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Cystic fibrosis mortality trends in France☆

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Abstract

Background: In 1992 France set up a national cystic fibrosis observatory (*Observatoire national de la mucoviscidose*, ONM) to monitor the state of health of patients on an annual basis. Using the ONM data, this study estimates the main indicators for life expectancy and assesses the total number of cystic fibrosis patients.
Methods: The data for the years 1994 to 2003 are divided into 3-year periods. Life tables are drawn up for these periods, from which mean and median lengths of life are determined. Using the most recent life table, the number of births in 2003 and the incidence of the disease, the total population of patients can be estimated, assuming a stationary population.
Results: In 2001–2003, life expectancy at birth of patients registered with the ONM was 39.1 years and median length of life was 36.4 years. These results, substantially better than those of 1994–1996, are linked to improved conditions of patient inclusion in the ONM database, to improvements in their healthcare, but also to the limitations of the life tables. Based on the 2003 data, the total theoretical number of patients is 6490, and coverage by the ONM database is thus 63.2%.
Conclusions: These provisional results demonstrate the need to convert the ONM observatory into a registry providing exhaustive coverage of all patients.

Keywords: Cystic fibrosis; Mortality; Life expectancy; Stationary population; Database; Observatory

1. Introduction

In most European countries as well as in North America, cystic fibrosis patients are living significantly longer thanks to improved disease management. Whereas only 20 years ago cystic fibrosis was essentially a paediatric problem, nowadays a steadily growing number of those affected are adults [1–3].

Despite the high incidence of this disease, estimated at 1 in 4600 births [4], France has only recently set up epidemiological monitoring of cystic fibrosis and organized specific healthcare structures. Two important decisions have been taken in this area however:

– Firstly, the creation in 1992 of a national cystic fibrosis observatory (*Observatoire national de la mucoviscidose*, ONM), initiated by the cystic fibrosis association, *Vaincre la Mucoviscidose*. Basically, the ONM's objectives are to improve knowledge of patients' medical and social characteristics, to measure the impact of treatment methods, to assess the socioeconomic cost of the disease, and to supply patients, their relatives and partner institutions with relevant information. The ONM works in association with treatment centres specialized in the management and follow-up of patients with cystic

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fibrosis. These centres receive funding from the *Vaincre la Mucoviscidose* association to take part in an annual collection of epidemiological data organized by the ONM. Since 1998, the ONM has been managed by the *Institut national d'études démographiques* (INED), a research institute which has been performing the ONM surveys and analysing the data obtained since 1999.

– Secondly, the decision by the Ministry of Health in October 2001 to introduce systematic neonatal screening for cystic fibrosis on a national scale [5]. This decision was accompanied by a procedure for recognition of existing treatment centres as cystic fibrosis specialist resource centres (*Centre de ressources et de compétences de la mucoviscidose*, CRCM) [6]. Universal screening of newborn babies was introduced in France in 2003 and the CRCMs are building up a network to structure and coordinate the care offered to patients, be they newborns detected by screening or patients diagnosed from symptoms occurring after birth. This national screening programme appears to confirm, for the moment, an incidence of the disease of 1 in 4600 births [7].

As the ONM is quite recent, mortality data had only been partially analysed until now [8,9]. In this article we will make a demographic analysis of the mortality of patients monitored by the observatory database and on that basis, estimate the total population of cystic fibrosis (CF) patients in France. Measuring mortality levels, like the total number of patients, may shed light on ways to improve the epidemiological observation tool currently available.

2. Materials and methods

2.1. Data collection

Data are collected via questionnaires sent once a year to the healthcare centres cooperating with the ONM in mainland France and Réunion Island. The information collected relates to the year just ended and concerns patients' identities, diagnostic data, demographic events occurring during the year, the method of medical follow-up, details of therapeutic management, anthropometric, spirometric and bacteriological parameters and some social data. For each annual survey, each participating centre reports on the patients seen at least once in the year. These patients may have already been seen by the centre the previous year or may have come for the first time during the year in question, either as new patients or following a transfer from another centre (these transfers are declared by clinicians for 2% of patients, and include transfers from paediatric centres to centres for adults). The reports submitted to the ONM by the centres concern:

– firstly, patients who have been clinically diagnosed with cystic fibrosis: the symptoms suggesting the disease, occurring in isolation or in association, are mainly bronchopulmonary and/or chronic ENT symptoms, exocrine pancreatic insufficiency, growth retardation and obstructive azoospermia [10,11];
– secondly, patients who do not necessarily exhibit the phenotypical signs of the disease: they may be newborn infants whose neonatal screening test was positive or subjects with a family history of the disease.

In all cases, the diagnosis of cystic fibrosis is confirmed by the sweat test (a concentration of chlorine in sweat above 60 mmol/l) and by detection of mutations of the CFTR gene.

The data examined in this article concern the deaths of patients who were included in the ONM database from 1994 (the date from which more than 70% of the centres in France contributed to the ONM) to 2003 (latest year for which survey information is available); the data from 1994 to 1998 are aggregate data supplied by the previous ONM manager, those from 1999 to 2003 are data on individuals collected directly by INED.

2.2. Analysis of mortality

The intensity of mortality was calculated using crude rates, measured as the ratio of the number of deaths to the mean population (the arithmetic mean of initial and final populations of each of the periods considered). These rates fluctuate substantially from year to year due to the small population size. To attenuate these fluctuations, the rates – although still expressing the mean annual numbers of events per 1000 patients – were established for periods comprising 3 consecutive years: 1994–1996, 1995–1997, 1996–1998, 1997–1999, 1998–2000, 1999–2001, 2000–2002, 2001–2003.

Mortality timing was measured by constructing abridged period life tables for each of the eight 3-year periods. These life tables give the following information:

– The number of deaths occurring between birthdays x and $x+5$, written as: $d(x, x+5)$.
– Five-year probabilities of dying, written as: ${}_5q_x$ which correspond to the probability of dying between birthday x and $x+5$. These probabilities were deduced from the various age-specific rates (5-year rates, written as: ${}_5m_x$) using the following equation: ${}_5q_x = 10 \times {}_5m_x/(2+5\times {}_5m_x)$.
– The number of survivors at age x, written as: S_x. Hence: $S_{x+5} = S_x - d(x, x+5) = S_x \times (1 - {}_5q_x)$.
– Life expectancy at age x, shown as: e_x, where $e_x = 2.5 + (5 \times (S_{x+5} + S_{x+10} + \ldots)/S_x)$. Considering the age reached by the last survivors, the maximum length of life for the study population was fixed at 80 years. For several 3-year periods, no death was actually observed after any patient's fiftieth birthday. In order to close the life tables, it was therefore necessary to work out a method for eliminating survivors in the 50- to 80-year-old age group. We opted arbitrarily for a regular extinction method, assuming that the intensity of mortality was likely to

increase with the age of the survivors. We also assumed that these deaths occurred in the middle of the 3-year period.

Thus constructed, the period life tables describe for each 3-year period what would happen to a synthetic cohort of newborn infants (arbitrarily limited to 1000 patients) who experience, as they get older, the mortality conditions of the period, and assuming zero migration (deaths of dropout patients are not taken into account here). The probability distribution is expressed in each life table as life expectancy at birth (indicator expressing the average number of years that a newborn exposed during his or her life to the risks of dying calculated for the 3-year period considered might expect to live), and median length of life (indicating the age that a newborn of the period theoretically has a 50% chance of exceeding) (Table 1, mortality 2001–2003).

Describing mortality conditions when there is migration of any kind involves taking dropouts into account. The latter have been correctly identified in the ONM database since 1999, the date from which individual-level data have been available to permit statistical monitoring of all patients included at least once in the database. On this basis, we consider that dropouts in a year n are those who were reported by a centre in year $n-1$, still alive on 31 December of year $n-1$ and not seen again, or not declared by any participating centre in any later year. To take account of dropouts during each of the 3-year periods, counting from 1999 to 2001, the initial probabilities of dying are adjusted by determining the ratio of the number of deaths $d(x, x+5)$ to the exposed population minus half the number of dropouts between birthdays x and $x+5$.

Table 1
Abridged life table

ONM population, 2003		Mortality, 2001–2003				Stationary population, 2003	
Age	n	$d(x, x+5)$	${}_5q_x$	S_x	e_x	${}_5p_x$	$P(x, x+4)$
0–4	687	1.00	0.0085	1000	39.1	0.996	827
5–9	654	3.00	0.0232	991	34.4	0.980	813
10–14	762	6.67	0.0431	968	30.2	0.948	787
15–19	681	10.33	0.0825	927	26.4	0.889	738
20–24	507	14.00	0.1456	850	23.6	0.789	655
25–29	360	11.00	0.1643	727	22.1	0.667	554
30–34	210	4.67	0.1256	607	21.0	0.569	472
35–39	120	3.67	0.2002	531	18.6	0.477	396
40–44	40	1.33	0.1554	422	17.8	0.390	324
45–49	38	0.67	0.1243	358	15.5	0.336	279
50–54	11	0.67	0.3137	313	12.4	0.265	220
55–59	12	0.33	0.1426	216	11.9	0.201	167
60–64	7	0.67	0.4511	185	8.4	0.142	118
65–69	10	0.33	0.2254	99	8.6	0.088	73
70–74	4	*3.50*	*0.4375*	77	*5.3*	*0.060*	50
75–79	1	*4.50*	*1.000*	*43*	*2.5*	*0.022*	18
80–84	0	*0*		*0*			0

Values in italics are estimations based on an arbitrary extinction method.

2.3. Estimating the total population of patients and its age structure in a stationary population

To estimate the population of patients, we adopt a stationarity model which serves solely to give a highly theoretical reference situation. We must make three assumptions for this purpose:

- a constant annual number of births (an assumption which holds true for France over the last 30 years). It is set at 761500, the number registered in 2003 in France [12];
- an incidence of cystic fibrosis at birth of 1 in 4600 (data confirmed by the latest systematic neonatal screening data). From these two parameters, we deduce an annual number (written as N) of 166 newborn infants suffering from cystic fibrosis;
- reference mortality as given by the 3-year life table for the period 2001–2003, which reflects the most recent situation of the ONM but which applies current mortality to all cohorts, including the oldest.

With the numbers supplied by the reference life table, the following values can be determined:

- The probabilities of survival between the ages x and $x+5$, shown as: ${}_5p_x$. Hence: ${}_5p_x=(S_x+S_{x+5})/2\times S_0$ where S_0 is the population of 1000 newborns given in the life table.
- The number of patients in the stationary population per age group, shown as $P(x, x+4)$. With the values accepted previously, the equation, per 5-year age group, becomes: $P(x, x+4)=(5\times N)\times {}_5p_x$.
- The total size of the stationary population, shown as P. This number is: $P=N\times e_0$ where e_0 is the life expectancy at birth given by the table (Table 1, stationary population 2003).

Under the stationarity assumption, the size of the population considered is constant. Moreover, the age structure of this population depends exclusively on the life table associated with it and remains constant over time [13].

3. Results

3.1. Characteristics of the ONM population

Between 1994 and 1999, the number of healthcare centres – i.e. separate hospital services – cooperating with the ONM rose from 59 to 91. The progressive creation of the CRCMs from 2000 to 2001 led to a grouping of certain services, thereby reducing the number of centres from 91 to 82 in 2003 (Table 2).

During this period, thanks to the improved service provided by the CRCMs, the number of patients treated in these centres increased steadily, rising from 2168 to 4104, with an average annual increase of 7.5%. The median age of ONM patients increased by 3.0 years, and the proportion of

Table 2
Characteristics of the ONM population

Characteristics	Years									
	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
Centres (*N*)	59	67	69	72	71	91	87	83	83	82
Patients (*N*)	2168	2524	2777	2937	2811	3220	3388	3580	3928	4104
Median age of patients (years)	11.0	11.6	12.0	12.0	13.0	13.0	13.0	14.0	14.0	14.0
Adults ≥ 18 (%)	23.9	27.2	29.4	30.1	33.1	32.8	34.5	35.5	37.1	37.9
Median age at diagnosis (months)	5.0	4.0	5.0	5.0	5.0	4.0	4.0	4.0	4.0	4.0
Genotype [a]										
ΔF508/ΔF508 (%)						58.4	56.7	55.3	54.2	52.6
ΔF508/other (%)						33.0	34.4	35.0	35.8	37.1
Other/other (%)						8.7	9.0	9.7	9.9	10.3
Taking pancreatic enzymes (%)	92.3	91.3	91.0	91.4	91.0	89.4	88.1	88.2	87.0	87.0
Mean FEV1 (% of predicted)	68.2	68.8	68.1	69.2	69.0	68.0	68.5	69.1	69.8	69.4
S.D. FEV1 (% of predicted)	27.4	27.1	27.9	28.2	28.3	27.7	27.4	27.6	27.8	27.4
Deaths (*N*)	46	55	54	75	63	44	45	53	66	56
Median age at death (years)	14.5	18.9	20.0	17.0	22.0	20.5	22.0	23.0	21.0	22.0

[a] Data available only for years 1999 to 2003.

adults (patients aged 18 and above) rose from 24% of ONM patients in 1994 to 38% in 2003. This substantial increase is doubtless the consequence of several factors, including the ageing of the cystic fibrosis population combined with improved disease management in the CRCMs for adults. The age at diagnosis remained stable, with half of all patients diagnosed before the age of around 4 months.

When the two mutations of the CFTR gene were identified (around 82% of patients), the most frequently observed genotype was ΔF508/ΔF508 (52.6% in 2003), with genotypes ΔF508/other and other/other representing respectively 37.1% and 10.3% in 2003. These frequencies are quite similar to those observed in most European countries.

In 1994, 92.3% of the ONM patients took pancreatic enzymes. This proportion fell progressively to 87% in 2003. The mean FEV1 appears to have remained quite stable throughout the study period, varying between 68% of the predicted value in 1999 and almost 70% in 2002.

In this type of rare disease, the number of deaths is naturally low. In the ONM, it rose from 46 in 1994 to 56 in 2003 but with major fluctuations from year to year, with a maximum of 75 in 1997. The median age at death, between 14.5 years in 1994 and 22.0 years in 2003, also fluctuates considerably, as it is dependent on the age structure of the study population and on its variations over the years. It is no more than indicative.

3.2. Characteristics of mortality

3.2.1. Intensity and timing of mortality (Table 3)

The crude death rate, which stood at 21.6‰ in 1994–1996, peaked at 23.9‰ in 1995–1997 then fell steadily to 15.8‰ in 2001–2003. Death rates by age group follow this overall trend, falling from 7.0‰ to 1.7‰ in the 0–4 age group and from 79.1‰ to 27.0‰ in the 45–49 age group between 1994–1996 and 2001–2003.

The indicators taken from the life tables, independent of the study population age structures, summarise mortality conditions for patients included in the ONM database more accurately than the above figures. Life expectancy at birth calculated for the period 1994–1996 is 30.4 years, and for 2001–2003 it is 39.1 years; life expectancy at age 20 (the mean number of years of life remaining for a patient who has survived to his or her twentieth birthday) is 16.7 years with the 1994–1996 data and reaches 23.6 years with the 2001–2003 data.

The distribution of survivors at the different birthdays and the associated indicators of median length of life clearly illustrate this change in the timing of mortality observed between the two periods at each end of the study (Fig. 1): a substantial difference is observed between the two survival profiles from the fifteenth birthday and this difference is then maintained. In the mortality conditions of the period 1994–1996, a newborn would have a one in two chance of exceeding 28.1 years of age, while in the mortality conditions of the period 2001–2003, a newborn would have a one in two chance of exceeding 36.4 years of age.

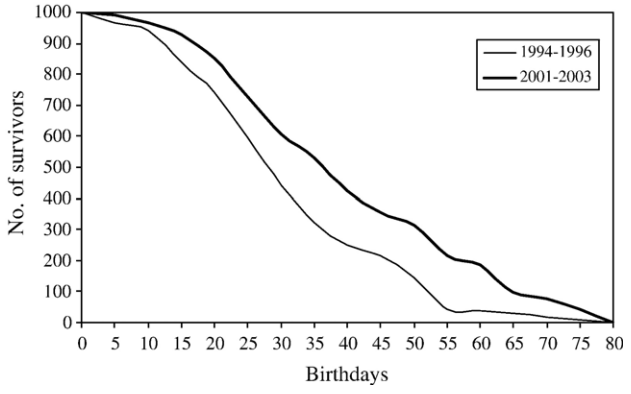

Fig. 1. Distribution of survivors according to age on birthdays. Periods of 1994–1996 and 2001–2003.

Table 3
Mortality characteristics of patients in the ONM database

Periods	Mortality indicators			
	Crude death rates (‰)	Life expectancy at birth (years)	Life expectancy at age 20 (years)	Median length of life (years)
1994–1996	21.6	30.4	16.7	28.1
1995–1997	23.9	30.9	18.1	27.8
1996–1998	23.4	32.0	18.5	28.1
1997–1999	21.3	34.0	20.4	29.6
1998–2000	16.8	37.1	21.6	32.2
1999–2001	14.7	39.0	23.0	35.7
2000–2002	15.8	38.0	22.4	35.6
2001–2003	15.8	39.1	23.6	36.4

Throughout the study period, most deaths (66.2%) were due to a respiratory cause; other correctly recorded main causes were cardiac (4.3%) and hepatic (1.3%) causes, trauma (1%) and suicide (1%).[1] When the primary cause is respiratory, quite frequently organ transplantation is a particular circumstance of death. During the period 2001–2003 for example, this was observed in 16% of cases.

3.2.2. Data corrected for dropouts

The number of dropouts over the 3-year period 1999–2001 was 251, i.e. 7.8% of the average reference population; the numbers were 222 for 2000–2002 (6.3% of the population) and 321 for 2001–2003 (8.7% of the population). For each of these three periods, nearly 80% of dropouts were under 25, the majority of them being in the 15–19 age group. Analysis of the FEV1 of all these dropouts shows that:

- this criterion is only available for 68% of them, compared with 72% of the full set of ONM patients over the same period (1999–2003);
- the means of the predicted value are 64.4 (years 1999–2001), 68.3 (2000–2002) and 76.2 (2001–2003); only this latter value is significantly higher than the mean observed for the entire ONM at the same period (Student's test: $p<0.001$); the health status of dropouts, on the basis of this criterion, does not appear to be very different from that of ONM patients overall.

Taking dropouts into account only slightly modifies the mortality indicators shown above (Table 3). For 2001–2003 for example, the crude death rate, which was 15.8‰, rises to 16.0‰ after correcting for dropouts (Table 4). Likewise, life expectancy at birth falls from 39.1 to 38.7 years and median length of life from 36.4 to 36.1 years.

[1] For all other reported causes, the proportion was below 1%. All these causes combined represent 17.2% of causes of death and 9.2% are non-documented causes.

Table 4
Mortality characteristics of patients in the ONM database corrected for dropouts

Periods	Mortality indicators			
	Crude death rates (‰)	Life expectancy at birth (years)	Life expectancy at age 20 (years)	Median length of life (years)
1999–2001	14.9	38.6	22.7	35.4
2000–2002	16.0	37.7	22.1	35.4
2001–2003	16.0	38.7	23.2	36.1

3.3. Estimating the total theoretical population of those affected

Assuming stationarity and taking life expectancy at birth to be 39.1 years, the theoretical total population of CF patients in France is an estimated 6490. As the number of patients actually observed by the ONM in 2003 was 4104, coverage by the observation tool is therefore 63.2%. The adjustment resulting from the inclusion of dropouts is minor: with a life expectancy of 38.7 years, the theoretical total population would be 6420 patients and coverage 63.9%.

Differences between the size of the observed population and that of the stationary reference population deduced from the latest life table vary substantially depending on age (Fig. 2). At age 10–14, the difference between the two series is very small, with a coverage rate of 96.8%; at age 0–4, the difference is quite large (687 patients observed versus 827 patients theoretically expected) and ONM coverage is 83.1%; at age 5–9, this difference increases slightly, and coverage is now only 80.4%. It is in the older age ranges (age 30 and above) that the differences in numbers become more pronounced. This is to be expected since the stationary model severely overestimates the survival of the oldest cohorts: at age 35–39, 120 patients are observed versus 396 predicted by the model, and likewise for the 50–54 age group, with 11 patients observed versus a predicted figure of 220.

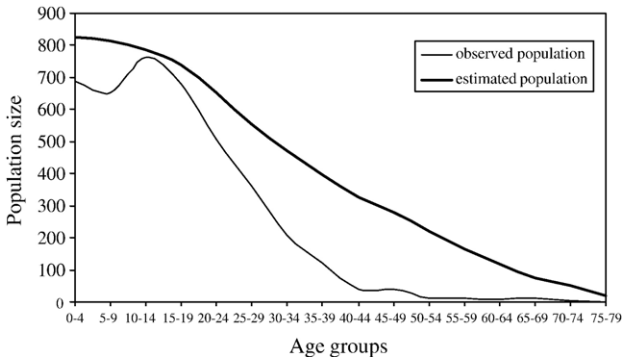

Fig. 2. Observed and estimated population by age. Year 2003; incidence at birth: 1 in 4600.

4. Discussion

Based on this demographic analysis, we can establish that over the recent period (2001–2003), life expectancy at birth of patients included in the database is around 39 years and median length of life is slightly above 36 years. However, despite the increasing number of patients included in the ONM database each year, the quality of the observation tool seems to be inadequate. Indeed, if incidence is 1 in 4600 births, then the 4104 patients recorded in 2003 represent only about 63% of the total population of CF patients estimated for a stationary population.

The increase in the life expectancy indicators between the two periods at each end of the study (+8.7 years life expectancy at birth and +8.3 years median length of life in 7 years), as well as their levels for the most recent period, should be interpreted with caution and doubtless overestimate the real situation. This can be explained by a number of factors:

- the data on which this analysis is based are not exhaustive. The surveys carried out each year by the ONM do not reach all patients since they only concern those consulting one of the healthcare centres cooperating with the ONM. As Fig. 2 illustrates, a considerable number of patients fall through the net, perhaps because they are treated outside the centres, or because they have not yet been diagnosed or because they suffer from a milder form of cystic fibrosis that does not require an annual medical check-up. As regards mortality data, information concerning patients who die outside the range of participating centres is therefore missing, as well as deaths in the first months of life when diagnosis has not yet been confirmed. Regarding this last category of deaths, the generalisation of systematic neonatal screening is still too recent for the deficits of the youngest patients to have been totally absorbed. Comparison of annual deaths observed by the ONM with those recorded by the *Institut national de la santé et de la recherche médicale* (INSERM) in the national database of deaths by cause [14] indicates that the level of under-reporting of deaths in the ONM is 14% for all ages. Under-reporting varies substantially between ages, but is most evident in the extreme age groups of 0–9 years on the one hand, and above 35 on the other (deficit of at least 30% on average compared with INSERM deaths). For certain years and certain age groups, ONM deaths are nonetheless over-reported with respect to INSERM deaths. These comparisons confirm the non-exhaustive nature of the OMS database, though the reliability of INSERM data on death by cause may also be uncertain.
- the gradual improvement in the level of ONM coverage over the years has produced a positive balance of observation entries with respect to dropouts, with a particular age structure. Generally speaking, the surpluses are found in the youngest age groups with the least risk of dying (in particular the group of 0–4 year olds) and deficits concern the adult age groups which, on the contrary, have the highest risk of dying. Overall, this balance therefore weighs in favour of delayed mortality timing. Over the last three periods of the study, the extent of this phenomenon was only very partially corrected by taking dropouts into account. Moreover, analysis of the proportion of patients taking pancreatic extracts (Table 2) appears to indicate a progressive increase, throughout the study period, of patients with a mild form of cystic fibrosis in terms of clinical symptoms. This tendency also appears to be confirmed by the decrease, from 1999 to 2003, in the proportion of patients with a homozygotic ΔF508 genotype, which again weighs in favour of reduced mortality. This reduced mortality may be attributable not to an actual improvement in health but rather to a progressive change in the composition of the study population.
- we introduced a certain amount of arbitrariness into the calculations of mortality at advanced ages (age 50 and above) in view of our chosen level of longevity; this is due to the inclusion of a patient aged 75 in the ONM database in 2000. Increasing longevity does not affect the values for median length of life but does modify the values for mean length of life (the maximum increase being 0.9 years when longevity is increased from 70 to 80 years).

Despite earlier reservations, cross-sectional analysis of mortality does have the basic advantage of producing various indicators which summarise the fatal events that affected the study population each year (or over a given period). However, life expectancy at birth and median length of life simply reflect mortality conditions at a given moment in time. One must beware, therefore, of thinking that the newborn infants in 2001–2003 will in fact survive on average for 39.1 years. This mean length of life will only be observed if the mortality conditions of the period 2001–2003 are maintained over the long term. The fate of the cohorts of patients born during the years 2001–2003 will very probably differ (as progress is made in treating the disease) from that of the synthetic cohort and from the instantaneous distribution of survivors that we constructed to measure the level of mortality for this period. Considering the low numbers observed and the limitations mentioned earlier, it would seem preferable to use the indicator of probable length of life (or median length of life) rather than that of mean length of life to compare France with other countries, although the methods used to measure mortality timing are sometimes very different [15,16]. The following median lengths of life are thus obtained for some of the countries that have cystic fibrosis databases: the United States (1999) 29.1 years [17], Canada (1985–1989) 27.8 years for women and 36.7 years for men [18], Great Britain (estimates for the present period based on 1994 data) about 30 years for women and 31 years for men [19],

Germany (1999) 31.6 years [20]. The former European registry for cystic fibrosis, which grouped together Germany, Belgium, Denmark, France, Great Britain, Ireland, the Netherlands and Sweden gave (for 1998) 32.0 years for median length of life [21]. An exploratory standardised study on mortality and related indicators undertaken by INED using data from France, Germany, Denmark, Italy and the United States has been very useful for comparing the differences in levels between these countries [22,23].

Estimating the total population of patients under the assumption of stationarity is only indicative, as no real population is strictly stationary. The stationary population must be considered as a reference population that can be used to assess, by comparison, certain concrete situations (as shown in Fig. 2). The calculations indicate that the ONM level of coverage may vary substantially from one age group to another. Under the stationarity assumption, we may consider these differences to be related to characteristics associated with the patients' age. Before 10–14 years, we observe a delay in diagnosis (in 2003, the median age at diagnosis was 4.0 months and the mean age, 37.7 months) and therefore a delay in entry into the ONM database; this delay will however gradually be absorbed by the implementation of neonatal screening. After 10–14 years, one can consider that the mortality of previous cohorts[2], much higher in reality than that described by the reference life table (2001–2003) – especially for advanced ages – partly explains the divergence between observed and predicted numbers. But there is also probably a large number of adult patients with mild forms of cystic fibrosis, who do not pass through the care centres. For their part, clinicians consider the large drop in levels of ONM coverage after age 15 to be rather unlikely and, consequently, also the estimate of the total adult population with the disease.

To conclude, it would seem essential to develop the observation tool currently available in France and to move on from a database, where registration of patients is incomplete, to a registry, in which inclusion and follow-up must be exhaustive. This should be possible, since newborn infants with the disease screened since 2002–2003 in France must be examined by a CRCM at least once a year. The inclusion of patients in this registry from birth will ensure reliable monitoring of their health status over the years and guarantee the robustness of a certain number of epidemiological indicators, notably that of mortality.

Achieving this objective calls for the creation of a multi-source structure to collect data on each patient. In addition to the standard healthcare structures, represented by the CRCMs, the following bodies could be involved:

- the organisation in charge of neonatal cystic fibrosis screening (AFDPHE),
- centres treating male sterility,
- the various state health insurance bodies, since all French people are covered by health insurance, whatever their economic status. They would provide a source of information on patients declared as having a long-term illness.

Only through concerted action of this kind will we develop our knowledge of cystic fibrosis in France.

[2] Who were born in 1987 or before as they were at least fifteen in 2002.

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